

**IN THE CLAIMS**

1. (previously presented) A method for screening a plurality of test substances useful for the prevention or treatment of a disease involving an oxidative stress, which comprises the steps of

i) testing each of the test substances for its ability to inhibit the activity of GADD34L and

ii) identifying the test substance which inhibits the activity of GADD34L, thereby to identify a test substance useful as a preventive or therapeutic agent for a disease involving an oxidative stress.

2. (previously presented) A method for identifying a test substance useful for the prevention or treatment of a disease involving an oxidative stress, which comprises testing a test substance for its ability to inhibit the activity of GADD34L, thereby to determine whether the substance promotes resistance to cell stress, and to identify said substance as a preventive or therapeutic agent for a disease involving an oxidative stress.

3. (previously presented) The method according to claim 1 or 2, wherein the test substance inhibits the activity of the GADD34L protein by disrupting formation of the GADD34L and PP1c protein complex.

4. (previously presented) The method according to claim 1 or 2, wherein the test substance inhibits the activity of GADD34L by inhibiting the production of GADD34L protein from the GADD34L mRNA.

5. (previously presented) The method according to claim 1 or 2, wherein the test substance inhibits the activity of GADD34L by inhibiting the production of GADD34L mRNA from the GADD34L genomic locus.

6. (currently amended) The method according to claim 2 ~~or 3~~, further comprising a step of verifying whether said test substance does not cause stress to cells.

7. (previously presented) The method according to claim 1 or 2, which comprises the steps of

i) contacting the test substance or each of the test substances with a cell-free composition containing GADD34L and PP1c proteins in the form of a purified complex and eIF2 $\alpha$  in a phosphorylated form,

ii) assessing the level of phosphorylation of eIF2 $\alpha$  in comparison with the level of phosphorylation determined in the absence of test substances, in a cell-free composition containing GADD34L and PP1c proteins in the form of a purified complex and eIF2 $\alpha$  in a phosphorylated form, and

iii) identifying the test substance which provides a higher level of phosphorylation of eIF2 $\alpha$ , in comparison with the level of phosphorylation determined in the absence of test substance, thereby to identify a test substance useful as a preventive or therapeutic agent for a disease involving an oxidative stress.

8. (previously presented) The method according to claim 7, wherein the assessment of the level of phosphorylation of eIF2 $\alpha$  is effected by an immunoassay using an antibody that specifically recognizes the phosphorylated form of eIF2 $\alpha$ .

9. (previously presented) The method according to claim 7, wherein the assessment of the level of phosphorylation of eIF2 $\alpha$  is effected by tracking the covalent binding of a radiolabelled phosphate group to eIF2 $\alpha$ .





20. (previously presented) The method according to claim 19, where the target gene is the CHOP gene.

21. (previously presented)      The method according to claim 1 or 2, which comprises the steps of,

i) obtaining cells not subject to stress that overexpress GADD34L, or portions thereof, and have been transfected with a reporter gene operatively associated with all or part of the promoter of a target gene,

ii) contacting a test substance or each of the test substances with these cells, and assaying the level of expression of said reporter gene, and

iii) identifying a test substance that activates the expression of the reporter gene, thereby to identify a test substance useful as a preventive or therapeutic agent for a disease involving an oxidative stress.

22. (previously presented) The method according to claim 21, where the target gene is the CHOP gene.

23. (previously presented) The method according to claim 21, wherein said reporter gene encodes one of the group consisting of GFP, CAT, GAL, LUC, and GUS.

24. (previously presented)      The method according to claim 1 or 2, which comprises the steps of,

- i) obtaining cells not subject to stress that overexpress GADD34L, or portions thereof,
- ii) contacting a test substance or each of the test substances with the cells, in the presence of a toxic agent that induces oxidative stress,

iii) quantitating cell survival of the cells that overexpress GADD34L, or portions of GADD34L, following exposure to the toxic agent in the presence and absence of test substances, and

iv) identifying a test substance that promotes cell survival of the cells following exposure to concentrations of toxic agent that induce oxidative stress, thereby to identify a test substance useful as a preventive or therapeutic agent for a disease involving an oxidative stress.

25. (previously presented)      The method according to claim 24 wherein the toxic agent which induces oxidative stress is tunicamycin, arsenite, or glutamate.

26. (previously presented)      The method according to claim 1 or 2, wherein the identified test substance is useful for the prevention or treatment of a disease involving neuronal ischemia.

27. (previously presented)      The method according to claim 1 or 2, wherein the identified test substance is useful for the prevention or treatment of a disease involving heart ischemia.

28. (previously presented)      The method according to claim 1 or 2, wherein the identified test substance is useful for the prevention or treatment of renal damage induced by ischemia or toxins.

29. (previously presented)      The method according to claim 1 or 2, wherein the identified test substance is useful for the prevention or treatment of an auto-immune disease.

30. (previously presented)      The method according to claim 1 or 2, wherein the selected compound is useful for the prevention or treatment of a neurodegenerative disorder.

31. (previously presented)      A method for the prevention or treatment of a disease involving an oxidative stress in a patient in need of such treatment, which comprises administering

to the patient an effective amount of a GADD34L inhibitor identified for its ability to promote resistance to cell stress while not causing stress.

32. (previously presented) A method of claim 31, wherein the disease is a disease involving neuronal ischemia, a disease involving heart ischemia, a disease involving renal damage induced by ischemia or toxins, an auto-immune disease, or a neurodegenerative disorder.

33. (new) The method according to claim 3, further comprising a step of verifying whether said test substance does not cause stress to cells.